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Isoprenaline as an aid to the induction of catecholamine dependent supraventricular tachycardias during programmed stimulation

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SUMMARY The effects of isoprenaline on the induction of supraventricular tachycardia by programmed stimulation were studied in 67 patients to see whether they correlated with spontaneous catecholamine mediated symptoms during exercise testing and Holter monitoring. Thirty seven control patients (group 1) did not have spontaneous arrhythmias either during exercise testing or Holter monitoring. Thirty patients (group 2) had documented exercise or stress related supraventricular tachycardias—that is paroxysmal junctional tachycardia (24) or atrial arrhythmia (6). Programmed electrical stimulation was performed before and during the infusion of isoprenaline. No group 1 patient developed sustained supraventricular tachycardia during isoprenaline infusion. In 21 patients with paroxysmal junctional tachycardia and all the patients with atrial arrhythmias electrical stimulation during isoprenaline infusion produced the same tachycardia that had been seen during exercise testing and Holter monitoring. Changes in electrophysiological variables and the concentrations of serum potassium were not associated with the induction of supraventricular tachycardia by isoprenaline. Infusion of isoprenaline safely facilitated the induction of supraventricular tachycardia by programmed stimulation in patients who had spontaneously occurring catecholamine mediated symptoms.

Although isoprenaline is known to facilitate the induction of ventricular tachycardia[1 2] it has rarely been used to aid the electrical induction of supraventricular tachycardia.

We report the results obtained when small infusions of isoprenaline were given to patients who did not have clinical supraventricular tachycardia and in whom standard stimulation techniques failed to induce tachycardia and to patients who did have spontaneous but non-inducible tachycardia.

Patients and methods

PATIENTS

Sixty seven patients who underwent programmed stimulation of the heart were classified according to the presence or absence of clinical and inducible supraventricular tachycardias.

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Group 1

Group 1 consisted of 37 patients aged from 12 to 67 (average 45) who had no clinical history of tachycardia. Seventeen had underlying heart disease: dilated cardiomyopathy (three), hypertrophic cardiomyopathy (five), coronary heart disease (two), mitral valve prolapse (two), congenital heart disease (four), valve disease (one). Four patients in group 1 had Wolff-Parkinson-White syndrome. Electrophysiological studies were performed to investigate the cause of syncope (12) or dizziness (17). These studies, which included ventricular stimulation, were also completed in eight patients with underlying heart disease (four cases) or were performed to assess the severity of Wolff-Parkinson-White syndrome (four cases). Twenty four hour Holter monitoring showed no evidence of supraventricular arrhythmias (three patients had atrial extrasystoles). No tachycardia or atrial extrasystoles were seen during upright bicycle exercise testing at an initial workload of 25 W, with subsequent increases of 25 W every two minutes. Exercise continued until exhaustion or the onset of symptoms.

No supraventricular tachycardia was induced by programmed stimulation in the basal state.

Group 2

Group 2 consisted of 30 patients aged from 15 to 80 (average 45) who had been admitted with supraventricular tachycardias and who had been included in a group of about 160 patients with supraventricular tachycardia studied in the laboratory over four years (1983 to 1987). Group 2a consisted of 24 patients with paroxysmal regular junctional reciprocating tachycardia and group 2b consisted of six patients with paroxysmal atrial arrhythmias—atrial fibrillation (two), atrial flutter (one), and atrial tachycardia (three). All the patients in group 2 had tachycardia induced by exercise or psychological stress. In most an electrocardiographic recording of the tachycardia was available. None the less, only eight of the 29 patients who exercised on the bicycle showed supraventricular arrhythmias during exercise. There were frequent salvoes of atrial extrasystoles (five), atrial tachycardia (one), and paroxysmal junctional tachycardia (two) immediately after exercise. Twenty four hour Holter monitoring in all the patients showed a paroxysmal junctional tachycardia in nine patients and atrial tachycardia in three patients. Nine patients had underlying heart disease: mitral valve prolapse (six), valvar heart disease (one), and dilated cardiomyopathy (two). Eight patients had Wolff-Parkinson-White syndrome. Electrophysiological study was performed to investigate the mechanism of the tachycardia (23) or syncope associated with tachycardia (seven).

All patients had normal serum concentrations of potassium. Cardioactive drugs were stopped at least five half lives before the study.

ELECTROPHYSIOLOGICAL STUDIES

Electrophysiological studies were performed in non-sedated patients in the post-absorptive state after they had given their informed consent. All patients were in normal sinus rhythm at the time of study. Right heart catheterisation was performed through the femoral vein with three 6 or 7 French multi-electrode catheters. Electrograms were recorded from the right atrium, the atrioventricular (AV) junction (His bundle electrogram), and the coronary sinus. Atrial and ventricular stimulation was performed with a programmable digital stimulator (Explorer 2000 Ela Médical) that delivered rectangular pulses lasting 1·8 ms at twice the diastolic threshold. Intracardiac electrograms and electrocardiographic leads I, III, and VI were simultaneously displayed on a multichannel oscilloscope (Siemens recording system) and recorded at a paper speed of 25 to 100 mm/s. Arterial blood pressure was measured by sphygmomanometry every five minutes.

We used the following protocol of programmed stimulation: (*a*) incremental atrial pacing up to the onset of type 1 second degree block; (*b*) atrial extrastimulus testing during sinus rhythm (S2) and atrial pacing at cycle lengths of 600 and 400 ms (S1 S2); (*c*) incremental ventricular pacing up to the onset of retrograde ventriculoatrial (VA) second degree or higher grades of ventriculoatrial block (maximal pacing rate 220 beats/min); (*d*) ventricular extrastimulus techniques up to S3 during sinus rhythm and ventricular pacing (cycle lengths of 600 and 400 ms) with two stimuli. In 21 patients the plasma concentration of potassium was measured after programmed stimulation in 21 patients.

Isoprenaline infusion was started at 0·5 μg/min and adjusted to increase the basal heart rate by at least 20%. In all patients the heart rate was increased to at least 100 beats/min (maximum of 150 beats/min). During the infusion we repeated the stimulation protocol and measured the serum concentration of potassium at comparable cycle lengths. The effective refractory periods were determined at a cycle length of 400 ms. The amount of isoprenaline required to induce the desired changes in heart rate ranged from 6 to 20 μg.

Heart rate and blood pressure were monitored continuously throughout the study.

DEFINITION OF TERMS

Non-sustained supraventricular tachycardia: at least five consecutive atrial extrasystoles, but less than one minute of tachycardia reproducibly induced.

Sustained supraventricular tachycardia: tachycardia that lasted more than one minute.

Non-sustained ventricular tachycardia: at least five consecutive ventricular extrasystoles, but reproducibly induced for less than one minute.

Sustained ventricular tachycardia: tachycardia that lasted more than one minute.

STATISTICAL ANALYSIS

We used a two tailed *t* test for independent or paired samples. Numerical data are presented as mean (1 SD).

Results

Tables 1–3 show the results of electrophysiological testing in all the study groups.

ELECTROPHYSIOLOGICAL VARIABLES (TABLE 4)

The effects of isoprenaline on heart rate and the AH and HV intervals were similar to those previously reported.[3] Isoprenaline shortened the length of the sinus cycle in group 1 and in group 2. It also

Table 1 *Results of electrophysiological study before and after infusion of isoprenaline (Iso)*

Case	Sex	Age (yr)	Indic	ECG	HD	ET	Holter	CL (ms)	AH (ms)	Ant 2nd° block (beats/min)	Retr block (beats/min)	A Stim	K+ (mmol/l)
1	M	60	S	N	HCM	—	—	850	120	100	0	—	
								Iso 500	60	160	200	—	
2	M	48	S	N	—	—	—	1000	70	160	0	—	
								Iso 470	50	190	200	—	
3	F	66	S	N	—	—	—	650	50	170	160	—	
								Iso 500	50	230	200	AESs	
4	M	67	S	SB	—	—	—	1300	75	120	90	—	
								Iso 650	70	190	100	—	
5	M	62	S	MA	CHD	—	—	750	70	205	0	—	
								Iso 550	60	230	0	—	
6	F	63	D	N	Valv	—	—	620	70	220	0	—	
								Iso 480	60	300	200	—	
7	M	51	D	SB	—	—	—	1100	80	100	100	E	3·9
								Iso 600	60	210	230	E	3·5
8	M	66	S	LBBB	—	—	—	780	70	160	160	—	4·3
								Iso 650	70	260	220	—	4·1
9	M	30	D	N	—	—	—	650	50	230	0	—	
								Iso 450	40	320	240	E	
10	M	37	D	N	—	VESs	VESs	550	60	240	210	NSAF	3·5
								Iso 400	30	290	220	—	3·4
11	F	62	D	N	HCM	—	—	1140	90	150	130	—	3·9
								Iso 600	80	230	220	—	3·9
12	M	46	S	N	—	—	—	920	100	170	110	E	3·8
								Iso 750	70	250	180	—	3·1
13	M	49	D	N	HCM	VESs	VESs	1000	40	210	130	E	4·3
								Iso 440	65	260	220	—	3·6
14	F	40	S	N	—	—	VESs	800	75	160	0	—	
								Iso 500	70	240	180	—	
15	M	35	S	N	—	VESs	VESs	800	100	140	0	NSAF	
								Iso 400	70	210	0	—	
16	F	64	D	N	—	—	VESs	1050	60	170	140	—	
								Iso 700	J	200	190	—	
17	F	36	D	N	RVD	—	VESs	650	50	240	0	E	
								Iso 450	40	300	200	—	
18	M	51	D	MI	CHD	—	—	870	80	170	170	—	
								Iso 550	60	250	200	—	
19	F	12	syst	RVH	cong	VESs	—	750	110	170	0	—	
								Iso 400	90	300	0	—	
20	M	61	syst	RBBB	HCH	—	VESs	650	75	190	110	—	
								Iso 550	75	250	220	—	
21	M	30	D	N	DCM	—	—	850	100	150	0	—	4·9
								Iso 500	60	230	0	—	3·7
22	M	56	S	N	—	—	VESs	660	100	150	0	—	
								Iso 500	60	230	0	—	
23	M	42	syst	LVH	DCM	—	VESs	600	40	200	170	—	3·6
								Iso 540	80	270	200	—	3·3
24	F	50	D	N	—	—	VESs	700	75	210	0	—	4·1
								Iso 450	60	230	220	—	3·7
25	F	16	D	N	RVD	VESs	VESs	750	100	150	0	NSAF	3·8
								Iso 380	80	280	240	—	3
26	M	56	D	N	—	—	—	850	120	100	0	—	
								Iso 500	60	160	200	—	
27	F	56	D	N	—	—	—	750	70	160	190	E	
								Iso 500	60	200	200	—	
28	M	17	S	N	MVP	—	VESs	950	90	150	100	—	
								Iso 500	70	210	150	—	
29	F	59	D	N	RVD	VESs	VESs	750	90	190	0	—	
								Iso 400	70	220	0	—	
30	M	46	S	LVH	HCM	—	—	950	95	170	0	—	
								Iso 510	65	220	120	—	
31	M	51	syst	LVH	DCM	—	—	620	80	180	190	—	3·7
								Iso 500	65	210	220	—	2·9
32	M	37	D	N	MVP	—	VESs	850	75	180	130	NSAF	4·6
								Iso 500	60	260	190	—	3·8
33	M	2	S	N	HCM	—	—	1050	70	110	0	NSAF	6·1
								Iso 550	55	250	190	—	4·6
34	M	37	syst	WPW	—	—	VESs	750	70	190	190	—	
								Iso 400	60	280	280	—	
35	F	25	syst	WPW	—	—	—	750	80	180	180	E	
								Iso 350	50	300	300	E	
36	M	35	syst	WPW	—	—	—	800	50	250	250	—	
								Iso 600	50	280	280	—	
37	M	14	syst	WPW	—	—	—	520	75	220	220	—	
								Iso 400	50	280	280	NSAF	

Indic (indication)—S, syncope; D, dizziness; syst, systematically (to study tachycardia induction).
ECG (electrocardiogram)—N, normal; SB, sinus bradycardia; MI, myocardial infarction; LBBB, left bundle branch block; LVH, left ventricular hypertrophy; RBBB, right bundle branch block; RVH, right ventricular hypertrophy.
HD (heart disease)—HCM, hypertrophic cardiomyopathy; CHD, coronary heart disease; RVD, right ventricular dysplasia; cong, congenital HD; DCM, dilated cardiomyopathy; MVP, mitral valve prolapse.
ET (exercise testing)—VES, ventricular extrasystole.
CL, cycle length; Ant 2nd° block, heart rate at which atrioventricular second degree block occurred; Retr block, heart rate at which ventriculoatrial block occurred; A Stim, results of programmed atrial stimulation; AES, atrial extrasystole; E, repetitive atrial echo beat; NSAF, non-sustained atrial fibrillation.

Table 2 *Patients with exercise related paroxysmal junctional tachycardias (group 2a)*

Case	Sex	Age (yr)	Indic	ECG	HD	ET	Holter	CL (ms)	AH (ms)	Ant 2nd block (beats/min)	Retr block (beats/min)	A Stim	K+ (mmol/l)
1	F	24	T	WPW	MVP	—	—	100	100	120	200	E	
								Iso 500	80	240	200	SPJT	
2	F	59	T	WPW	—	—	—	900	90	140	190	—	
								Iso 450	60	250	200	SPJT	
3	M	28	T	N	—	—	—	800	90	160	0	—	
								Iso 450	60	260	200	—	
4	M	55	T	N	—	—	—	900	70	185	150	—	
								Iso 500	60	210	200	SPJT	
5	M	31	T-S	N	—	—	—	870	90	180	140	NSAT	
								Iso 450	70	250	200	SPJT	
6	M	57	T	WPW	MVP	—	PJT	1000	70	150	200	NSPJT	
								Iso 450	60	250	200	SPJT	
7	F	33	T-S	WPW	—	—	—	750	60	150	180	E	
								Iso 350	45	300	200	NSPJT	
8	F	33	T	WPW	—	—	—	1000	130	120	160	NSPJT	
								Iso 500	70	230	200	SPJT	
9	F	60	T-S	WPW	—	—	—	700	80	180	160	NSAFI	
								Iso 450	50	240	200	SPJT	
10	M	34	T	RBBB	MVP	—	PJT	960	90	150	0	—	
								Iso 500	70	250	170	SPJT	
11	F	80	T-S	N	—	?	PJT	600	90	170	0	NSAT	
								Iso 500	80	190	160	SPJT	
12	M	15	T	N	—	—	—	860	70	145	170	—	
								Iso 500	50	210	200	SPJT	
13	F	61	T	N	MVP	—	PJT	1000	130	135	170	NSPJT	
								Iso 700	70	230	200	SPJT	
14	M	33	T	N	—	—	—	770	75	215	180	NSPJT	
								Iso 550	60	240	240	SPJT	
15	M	29	T	WPW	—	PJT	PJT	800	60	160	210	—	
					—	(post ET)		Iso 420	40	230	210	—	
16	F	31	T	N	—	—	—	660	110	170	120	O	
								Iso 500	60	270	220	SPJT	
17	M	26	T	N	—	—	—	800	80	150	180	E	4·2
								Iso 420	50	250	240	SPJT	2·7
18	M	46	T	LVH	DCM	AESs	PJT	640	90	220	200	—	4
								Iso 420	70	240	200	SPJT	3·5
19	M	52	T	LVH	DCM	—	VESs	800	70	150	150	NSA fl	4·5
								550	60	210	220	SPJT	3·5
20	M	64	T-S	N	—	AESs	AT	750	60	230	180	E	3·4
								Iso 450	45	310	230	SPJT	3·5
21	F	45	T	N	—	—	PJT	710	75	220	150	NSAF	3·5
							VT	Iso 400	35	280	240	SPJT	3·3
22	F	33	T-D	WPW	—	PJT	PJT	800	45	210	130	NSAF	3·5
						(post ET)		Iso 430	40	290	220	SPJT	3·3
23	F	61	T	N	MVP	—	NS PJT	1000	140	140	0	NSAFI	4·1
							VESs	Iso 570	90	210	160	SPJT	2·7
24	F	43	T	N	—	—	—	720	60	200	170	NSPJT	3·4
								Iso 500	60	300	>240	SPJT	3·4

WPW, Wolff-Parkinson-White; AT, atrial tachycardia; PJT, paroxysmal junctional tachycardia; S, sustained; NS, non-sustained; AF, atrial fibrillation; A fl, atrial flutter. See footnote to table 1 for other abbreviations.

Table 3 *Results of electrophysiological study before and after infusion of isoprenaline in patients with exercise related paroxysmal atrial arrhythmias (group 2b)*

Case	Sex	Age (yr)	Indic	ECG	HD	ET	Holter	CL (ms)	AH (ms)	Ant 2nd block (beats/min)	Retr block (beats/min)	A Stim	K+ (mmol/l)
1	F	49	T	N	MVP	—	—	900	70	140	0	E	
								Iso 500	60	—	160	SAfl	
2	M	50	T	N	—	AESs	—	700	90	210	150	—	
								Iso 600	80	240	200	SAF	
3	F	56	T-S	LVH	Valve	AESs	—	800	80	130	110	NSAF	
								Iso 500	60	230	200	SAF	
4	M	61	T	N	—	AT	—	1000	120	105	0	—	
								Iso 480	120	2nd AVB	0	SAT	
5	M	66	T	N	DCM	AESs	AT	770	60	160	110	NSAT	3·5
								Iso 640	60	280	220	SAT	3·5
6	M	47	T	1st AVB	—	AESs	AT	1100	130	90	90	NSAT	
								Iso 800	70	170	?	SAT	

AVB, atrioventricular block. See footnotes to tables 1 and 2 for other abbreviations.

Table 4 *Electrophysiological variables (mean (1SD) before and after isoprenaline (Iso)*

	CL (ms)	*AH (ms)*	*Ant 2nd° block (beats/min)*	*Retr block (beats/min)*	*K^+ (mmol/l)*
Group 1:					
Before	812 (75)	82 (21)	173 (39)	104 (51)	4·2 (0·7)
Iso	505 (91)	62 (13)	243 (40)	177 (64)	3·6 (0·7)
p	< 0·001	< 0·001	< 0·001	< 0·001	< 0·03
Group 2:					
Before	832 (123)	86 (23)	169 (32)	143 (52)	3·9 (0·4)
Iso	485 (70)	63 (18)	245 (31)	204 (37)	3·3 (0·4)
p	< 0·001	< 0·001	< 0·001	< 0·001	< 0·01

shortened the AH interval in group 1 and in group 2 and had no effect on the HV interval. Isoprenaline reduced the atrial effective refractory period calculated at a driven atrial rhythm of 400 ms in both group 1 (218 (12) ms *v* 171 (14) ms, $p < 0·01$) and group 2 (209 (16) ms *v* 165 (19) ms, $p < 0·01$). The atrial rate at which anterograde type 1 second degree block developed increased significantly in group 1 and group 2. The ventricular rate at which retrograde second degree block developed increased significantly in group 1 and group 2. Isoprenaline reduced the ventricular effective refractory periods calculated at a driven rhythm of 400 ms from 210 (5) ms to 175 (7) ms ($p < 0·01$) in group 2 and from 202 (7) ms to 173 (5) ms ($p < 0·01$) in group 2. The effects of isoprenaline on the anterograde and retrograde refractory periods of Kent bundles were similar to those reported elsewhere[4]: isoprenaline generally shortened the refractory periods in patients with the longest initial values (average 50 ms).

SERUM CONCENTRATIONS OF POTASSIUM

The serum concentration of potassium fell significantly in group 1.

INDUCED SUPRAVENTRICULAR TACHYCARDIA

In the basal state sustained supraventricular tachycardia could not be induced by programmed stimulation in any patient; a non-sustained atrial arrhythmia was induced in five patients from group 1 and in eight from group 2 and a non-sustained paroxysmal junctional tachycardia was induced in five patients from group 2.

After infusion of isoprenaline sustained supraventricular tachycardia could not be initiated in any group 1 patients, even when they had had non-sustained supraventricular tachycardia during the basal study. Non-sustained atrial tachycardia was induced in one group 1 patient who did not have inducible arrhythmia in the basal state.

After isoprenaline sustained junctional tachycardia was induced in 21 patients in group 2a either spontaneously (three) or by programmed stimulation (18). There were 13 re-entrant tachycardias in the atrioventricular node and eight re-entrant tachycardias conducted retrogradely through a Kent bundle. Non-sustained junctional tachycardia was induced in one patient.

After isoprenaline, clinical sustained atrial tachycardia could be reproduced in six patients in group 2 either spontaneously (three) or by programmed stimulation (three). There was one atrial flutter, two atrial fibrillations, and three atrial tachycardias.

In group 2 the sensitivity of the isoprenaline test, defined as the percentage of inducible sustained supraventricular tachycardia, was 90%. Specificity, defined as the percentage of negative tests, was 100% in group 1.

CORRELATION BETWEEN JUNCTIONAL TACHYCARDIA AND ELECTROPHYSIOLOGICAL VARIABLES AND SERUM POTASSIUM (TABLE 5)

We analysed certain variables in patients in group 2a and group 1 to discover whether any of them correlated with the induction of junctional tachycardia.

After isoprenaline we did not find any differences between groups 1 and 2a for variation in cycle length, AH interval, heart rate at which anterograde type 1 second degree block developed, and serum potassium. In group 2a retrograde block was significantly more common after electrophysiological testing in the basal state ($p < 0·05$) and after isoprenaline ($p < 0·02$) (fig). However, the occurrence of a fast retrograde conduction after isoprenaline did not assist the prediction of the induction of junctional tachycardia: seven patients from group 1 without retrograde conduction in the basal state showed retrograde conduction on isoprenaline at stimulation rates of up to 200/min. The sensitivity of the isoprenaline test defined as the percentage of patients in whom retrograde conduction developed at stimulation rates of 200/min was 86% in group 2a, but its specificity, defined as the percentage that developed retrograde conduction at rates of <200 beats/min was 38% in group 1.

Table 5 *Electrophysiological variables (mean (1SD) before and after isoprenaline in groups 1 and 2a*

	Group 1	*Group 2a*	*p*
CL (ms):			
Before	812 (75)	832 (131)	
Iso	505 (91)	483 (73)	NS
AH (ms):			
Before	82 (21)	86 (23)	NS
Iso	62 (13)	63 (18)	NS
Ant 2nd° block (beats/min):			
Before	173 (39)	169 (35)	NS
Iso	243 (40)	245 (33)	NS
Retr block (beats/min):			
Before	104 (51)	144 (65)	< 0·005
Iso	177 (64)	212 (25)	< 0·02
K^+ (mmol/l):			
Before	4·2 (0·7)	3·9 (0·4)	NS
Iso	3·6 (0·5)	3·3 (0·4)	NS

CL, cycle length; Ant 2nd° block, heart rate at which atrioventricular second degree block occurred; Retr block, heart rate at which ventriculoatrial block occurred; K^+, serum concentration of potassium.

ADVERSE EFFECTS OF THE ISOPRENALINE TEST

Arterial blood pressure fell significantly in only one patient. Three patients in group 1 and one in group 2 showed transient sinus bradycardia and a fall in blood pressure several minutes after the beginning of isoprenaline infusion; one of these patients had spontaneous salvoes of atrial tachycardia.

One patient from group 2 had spontaneous non-sustained uniform ventricular tachycardia (130 beats/min). The systematic programmed ventricular stimulation induced non-sustained multiform ventricular tachycardia in the basal state in two patients in group 1 and four in group 2. After isoprenaline, none of the patients from group 1 and only two from group 2 had induced multiform non-sustained ventricular tachycardia.

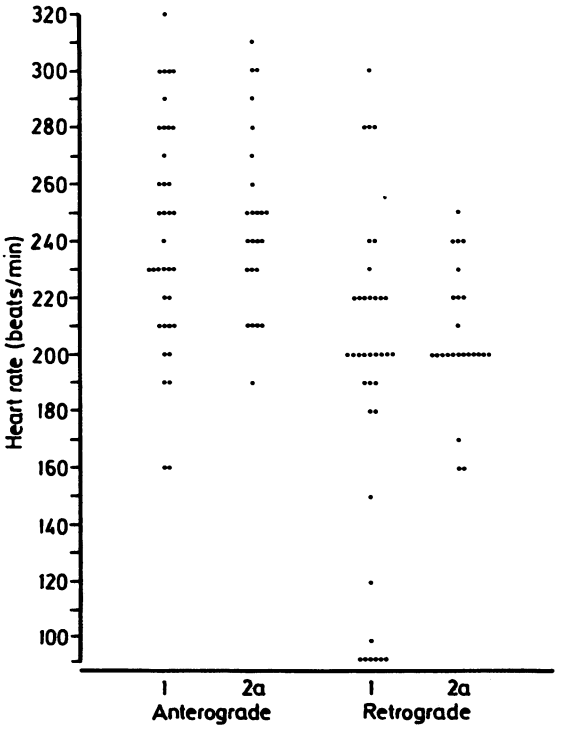

Figure *Heart rates at which anterograde and retrograde type 1 second degree block developed during isoprenaline infusion in groups 1 and 2a.*

Discussion

We found that the isoprenaline test assisted the diagnosis of catecholamine mediated junctional tachycardias (sensitivity 90%, specificity 100%).

The role of the sympathetic nervous system in supraventricular arrhythmias was suggested by clinical observations, the bicycle exercise test, and 24 hour Holter monitoring.[5] Adrenergic supraventricular tachycardias are induced by exercise or stress, and they occur predominantly during the day. There have been few studies of adrenergic supraventricular tachycardia. The role of adrenergic effects, which modify the refractory periods of accessory pathways, has been studied mainly in Wolff-Parkinson-White syndrome.[4,6,7] Coumel *et al* reported Holter studies to evaluate the role of the sympathetic nervous system in arrhythmias other than in the Wolff-Parkinson-White syndrome.[5] In our study, the sensitivity of Holter monitoring for the diagnosis of adrenergic supraventricular arrhythmia was poor (40%). The sensitivity of exercise testing for triggering a supraventricular tachycardia was also poor (40%). Moreover, when tachycardia occurs immediately after exercise during Holter monitoring, as in cases 15 and 22, the mechanism could be adrenergic or vagal.[8]

These findings indicated the desirability of a pharmacological test that induced trachycardias caused by adrenergic mechanisms. In patients with exercise induced ventricular arrhythmias isoprenaline often caused identical arrhythmia.[9,10] Isoprenaline produces β adrenergic stimulation, which affects the electrophysiological properties of the single cell and the intact heart in several ways.[1-11] In single fibres isoprenaline increased the spontaneous phase IV depolarisation of sinus node, facilitated the development of triggered automaticity, and shortened the action potential duration. In intact hearts, isoprenaline increased the sinus rate and the rate of ectopic pacemakers, accelerated atrioventricular conduction, and shortened the refractoriness of the atrioventricular node and His-Purkinje system. It might be difficult to establish whether the tachycar-

dia induced by isoprenaline resulted from direct stimulation of cardiac β adrenoreceptors or from reflex changes, which might be in the opposite direction, depending on whether the blood pressure rose or fell.[12] Vagal tone may be increased, as in three of our patients, or reduced by the haemodynamic effects of isoprenaline.

An alternative approach to the adrenergic initiation of tachycardia is to use atropine to withdraw the vagal effect, leaving the action of natural catecholamine unopposed. A pharmacological test could also be based on adrenaline, noradrenaline, and atropine.

The frequency with which isoprenaline facilitates the induction of atrial tachycardia has not been reported before. In our study there were six patients with an adrenergic mediated tachycardia that could be reproduced by infusion of isoprenaline and electrophysiological stimulation. The spontaneous occurrence of the arrhythmia in three of them may implicate enhanced automaticity. Non-sustained atrial tachycardia was induced in only one of the controls. Thus infusion of isoprenaline seems a useful provocative test to detect adrenergic paroxysmal atrial tachycardia.

There are few studies of the frequency with which isoprenaline facilitates the induction of junctional tachycardia. Levy *et al* and Hariman *et al* reported two cases of catecholamine dependent atrioventricular nodal reentrant tachycardia[13,14]; Hariman *et al* proposed the enhancement of ventriculoatrial conduction as the mechanism of these tachycardias.[14] In our study, this mechanism was not confirmed. Most reports deal with the induction of junctional tachycardia associated with the Wolff-Parkinson-White syndrome. The spontaneous initiation of reciprocating tachycardia in the Wolff-Parkinson-White syndrome by isoprenaline infusion was reported by Krikler *et al*.[15] Kuck *et al* found a strong correlation between the results of isoprenaline infusion at rest and the results of an exercise test,[16] and in five patients with exercise induced junctional tachycardia, isoprenaline infusion identified the arrhythmia. On the other hand, Brugada *et al* did not find any correlation between the occurrence of isoprenaline induced tachycardias and exercise induced tachycardia.[17] The same results were reported for supraventricular tachycardias.[12] The effects of isoprenaline and exercise on the facilitation of arrhythmia do not always coincide: isoprenaline facilitated the induction of arrhythmia in patients with sustained ventricular tachycardia not related to exertion.[2]

In patients who did not have Wolff-Parkinson-White syndrome or spontaneous arrhythmias, we did not find that infusion of isoprenaline increased the induction of non-sustained atrial or ventricular tachycardia. The mechanism by which isoprenaline facilitates the induction of junctional tachycardia remains unknown. Triggered automaticity and delayed after-depolarisation were possible mechanisms for the tachycardia that occurred during isoprenaline infusion in the two patients with spontaneous junctional tachycardia. In the study of Krikler *et al* incessant attacks of tachycardia without antecedent PR prolongation were induced by isoprenaline and were attributed to the speeding of the sinus rate, which might sufficiently shorten the refractory periods of the atrial and anomalous pathways to permit retrograde conduction up the anomalous pathway to the atrium thus causing an echo beat and tachycardia.[15] In most of our patients ($n = 19$), the arrhythmias required an initiation beat and were stopped by one or two stimuli, suggesting that isoprenaline infusion facilitated reentry by reducing the refractoriness and increasing conduction velocity and the myocardium. The induction of catecholamine dependent reentrant tachycardia has been attributed to a rapid anterograde and/or retrograde conduction[14,18]; this explanation was not confirmed in our study.

Because adrenaline can reproduce stress hypokalaemia[19,20] another mechanism by which isoprenaline might have facilitated reentry was by a reduction in intracellular potassium. The fall in serum potassium, however, was similar in groups 1 and 2, so this mechanism cannot account for the facilitation of arrhythmia.

Infusion of isoprenaline can safely be used to facilitate the induction of supraventricular tachycardia in patients who have spontaneous supraventricular tachycardia, when sympathetic stimulation is enhanced.

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